REMARKS

Claims 12-13, 18-26, 44-49 and 52-84 are pending. Claims 50-51 have been canceled. Claims 85-122 are new. Claims 12, 52-56 and 67-70 have been amended. No new matter is added by the amendments.

Claim 12 has been amended to recite specific bases for Base*. Support for this amendment is found on pages 105-106 of the specification.

Claims 52-56 and 68-70 have been amended to recite "Base*" and to delete the terms "purine base" or "pyrimidine base."

Claim 67 has been amended to delete reference to the group Base*.

Claims 50-51 and 67 have been amended to recite "Base*" in reference to claim 12 from which each of claims 50, 51 and 67 depend.

New claim 85 recites a method for the treatment of a host infected with a hepatitis C virus, comprising contacting a hepatitis C virus in the host with a compound of the formula provided. This claim is supported by, for example, the specification at page 12.

New claims 86-120 depend from new claim 85, and are based on previously presented claims 12-13, 18-26, 44-49 and 52-82. Support for these claims may also be found, for example, in the specification at pages 44-46.

New claims 121-122 recite the compounds of previously presented claim 12, and are supported by, for example, the specification at page 59.

Claims 12-13, 18-26, 44-49 and 52-84 stand rejected. Applicants respectfully request reconsideration of the pending rejections based on the amendments and the following comments.

Claims Rejections under 35 U.S.C. § 112, First Paragraph

Claims 12-13, 18-26 and 44-84 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking enablement. Citing *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988), the Examiner alleges that the specification does not reasonably provide enablement for the treatment of hepatitis C virus ("HCV") with compounds wherein Base* is a purine or pyrimidine base. (Office Action, page 3). Specifically, the Examiner relies on the following *Wands* factors: (1) the breadth of the claims/nature of the invention, (2) the level of predictability in the art, (3) the amount of direction provided by the inventor, (4) the existence of working examples, and (5) the quantity of experimentation needed to make and use the invention. (Office Action, pages 3-4). Applicants respectfully traverse this rejection.

1. The breadth of the claims/nature of the invention.

The Examiner alleges that the instant claims lack enablement because the methods of the claims encompass thousands of compounds, as the definition of Base* is "purine or pyrimidine base." (Office Action, page 3). Solely to promote prosecution and without prejudice, claim 12 has been amended to recite the specific groups disclosed in the specification for Base* at pages 105-106. Therefore, the breadth of compounds encompassed by claim 12 is substantially smaller than those originally claimed.

2. The level of predictability in the art.

The Examiner cites Clark, *et al.*, Bioorganic & Medicinal Chemistry Letters, 16, 1712-15 (2006) ("Clark") to allegedly demonstrate that the level of unpredictability in the art is high. (Office Action, page 4). Specifically, the Examiner alleges that Clark "teaches that only those 2'-deoxy-2-fluoro-2'-C-methyl nucleosides with a 2-amino group on the purine base reduced levels of HCV RNA in a subgenomic replicon assay." *Id.* Applicants disagree. In Clark, the author concludes that the data "suggests that both the 2-amino and 2'-β-methyl groups are important substituents for *selective* HCV inhibition...." (Clark, page 1714) (emphasis added). Compounds 2 and 11 of Clark, which do not contain a 2-amino group on the purine base, exhibit comparable potency against HCV to compounds 1, 13 and 14, which do contain the 2-amino group. Clark simply teaches that the 2-amino group may be important for *selective* HCV inhibition, not HCV inhibition itself. Therefore, because the instant claims are directed to methods of treating HCV in a host, without regard to selectivity, Clark does not support the Examiner's allegation that the 2-amino is essential to predictability in the art.

Furthermore, in Clark, only six compounds were tested in a single specific HCV assay. These results alone do not demonstrate that the selection of base substituents on 2'-C-methyl nucleosides for the treatment of HCV infections is unpredictable. Indeed, the Examiner's suggestion that the 2-amino group is essential for predicting HCV activity in the compounds of the instant claims is contradicted by what is known in the art. For example, U.S. Patent No. 6,812,219 teaches that 2'-C-methyladenosine, 2'-C-methylthymidine, 2'-C-methyluridine, 2'-C-methylcytidine, 2'-C-methylguanosine and 2'-C-methylinosine are active against Bovine Viral Diahrrea Virus, which is a well known surrogate for hepatitis C virus. *See* V.E. Buckwold, *et al.*, "Bovine viral diarrhea virus as a surrogate model of hepatitis C virus for the evaluation of antiviral agents." *Antiviral Research,* 60: 1–15 (2003) (copy enclosed). This reference demonstrates that a variety of nucleoside bases may be used in 2'-C-methyl nucleosides for the treatment of HCV. Applicants respectfully point out to the Examiner that the present invention

is based on the selection of substituents at the '2-postion of the ribose ring,which is not predictable, not in the selection of a nucleoside base. Therefore, because the level of predictability in the art with respect to base selection for the compounds of the instant claims is high, the methods of the instant claims have been enabled by the instant specification.

3. The amount of direction provided by the inventor.

The Examiner alleges that the specification does not provide adequate guidance for one skilled in the art "to use the claimed method[s] commensurate in scope with the instant claims." *Id.* However, the Examiner does admit that the claims are enabled for the treatment of HCV with compounds wherein Base* is a purine with "a 2-amino group on the purine base...." (Office Action, pages 2-3). Claim 12 has been amended to recite a list of specific nucleoside bases for Base*. The balance of the claims, which depend from claim 12, recite further limitations of the compounds of the claimed methods. The scope of the instant claims is sufficiently narrow such that one skilled in the art, following the instant specification, could practice the methods of the instant claims.

Furthermore, the specification teaches that the compounds disclosed therein are active against *Flaviviridae* viruses, including HCV, at page 12. This teaching is supported by what is currently known in the art of 2'-C-methyl nucleosides as inhibitors of HCV. For example, US Patent Publication No. 2005/0009737 teaches that 2'-C-methylcytidine, 2'-fluoro-2'-C-methylcytidine and 2'-C-methyladenosine exhibit activity against HCV. These teachings demonstrate that many different nucleoside bases may be present in 2'-C-methyl nucleosides active against HCV. Therefore, one skilled in the art would expect that the base substituent of the compounds of the instant methods can be varied without eliminating the anti-HCV activity of these compounds.

4. The existence of working examples.

The Examiner points out that the specification does not provide any examples in which the claimed compounds are tested for activity against HCV. (Office Action, page 4). "The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation." MPEP § 2164.02 (*citing In re Borkowski*, 422 F.2d 904, 908 (C.C.P.A. 1970)). Applicants respectfully point to the references cited above, which demonstrate the activity of a number of compounds within the scope of the instant claims. These disclosures,

along with the teachings of the instant specification, enable one skilled in the art to practice the claimed methods without undue experimentation. *Id.*

5. The quantity of experimentation needed to make and use the invention.

The Examiner alleges that one skilled in the art "would be confronted with an undue burden of experimentation to isolate, characterize, and test the group of compounds of claim [12]...to determine if indeed they have efficacy as anti-HCV agents." (Office Action, pages 4-5). Applicants disagree.

First, Applicants point out that instant claim 12 has been amended such that Base* is no longer "a purine or pyrimidine base" but a specific group of purine and pyrimidine bases. Therefore, the scope of compounds recited in the instant methods is substantially smaller than in the previously pending claims, thereby greatly reducing the potential amount of experimentation.

Second, the instant specification provides working examples of the preparation of many of the compounds of the pending claims. (*See* Examples 1-24, pages 134-154). One skilled in the art would be able to prepare the balance of the compounds of the instant claims based on the disclosure in the above-mentioned examples without undue experimentation.

Third, as shown above, the art contains examples of 2'-C-methyl nucleosides and 2'-fluoro-2'-C-methyl nucleosides with demonstrated anti-HCV activity. One skilled in the art would expect the compounds of the instant claims to have anti-HCV activity, and could easily follow the examples provided in the art to test these compounds. Thus, the amount of experimentation to test the compounds of the instant claims would not be undue with these references, and the teachings of the instant specification in hand.

Therefore, for at least these reasons, the instant claims, as presently amended, are enabled by the instant specification in view of the state of the prior art. Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

CONCLUSION

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested.

No fee is believed due for this submission. However, should any fees be due for this submission or to avoid abandonment of the application, please charge such fees to Jones Day Deposit Account No. 503013.

If the Examiner believes it would be useful to advance prosecution, the Examiner is invited to telephone the undersigned at (858) 314-1200.

Respectfully submitted,

Date: August 20, 2007

Dale Rieger Reg. No. 43,045

JONES DAY
222 East 41st Street
New York, New York 10017
(858) 314-1200